



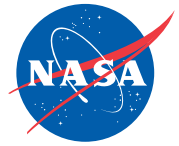
18. Certifying a Sterilization Process: A Regulatory Pathway

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The decision to implement Mars Sample Return will not be finalized until NASA's completion of the National Environmental Policy Act (NEPA) process. This document is being made available for information purposes only.
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Define a process for certification for use in Backward PP



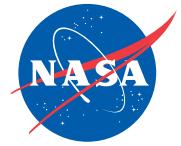
Mars Sample Return Pre-Formulation

- **Planetary Protection** addresses microbial contamination of the solar system:
 - Spacecraft that we launch from Earth (forward contamination)
 - Contamination of the Earth and Moon (backward contamination), from restricted sample return missions
- To prevent either forward or backward contamination, spacecraft hardware must be cleaned and/or sterilized then evaluated for the presence of microorganisms.
 - Cleanroom environments
 - Cleaning the hardware
 - Routinely sample the cleaned hardware

“Certifications” for backward PP

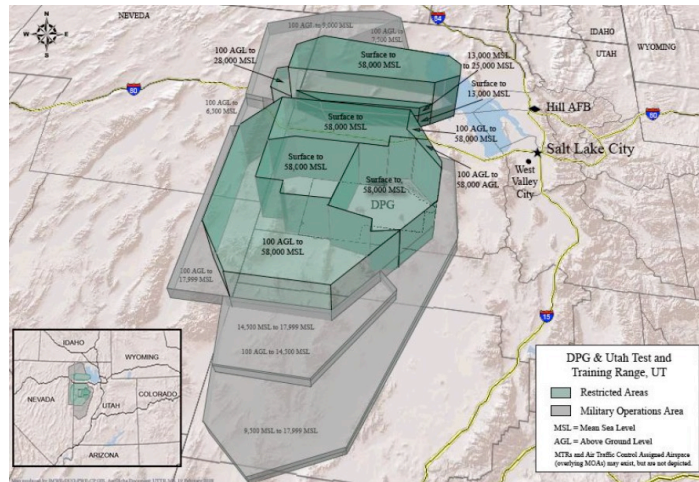
- Breaking the Chain/Sterilizing the OS would occur before EDL on Earth and receiving in a notional MSRH.
- To gain launch or landing approval for MSR, NASA must gain regulatory approval from several federal agencies certifying that the environmental impact will be controlled and risk minimized to an acceptable level.

UTTR – Potential Landing Site Under Consideration



Mars Sample Return Pre-Formulation

- The DoD controls the airspace around the potential landing site at Utah Test and Training Ranges (UTTR).
 - UTTR - Largest overland contiguous block of restricted airspace in the continental United States. The airspace, situated over 6,796 square kilometers (2,624 square miles), is under the jurisdiction of the U.S. Air Force.
 - supersonic flight,
 - aircrew training
 - weapons testing.
 - The Army controls Dugway Proving Ground (DPG) which during the Genesis mission was used to stage an ISO 5 cleanroom prior to transport to JSC



DPG and UTTR Footprint and associated airspace



Genesis clean room at DPG

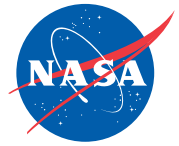
- Some applicable regulations necessary for DoD to approve landing site
 - Trajectory analysis – Understand impact, targeting guidance, and landing ellipse
 - BSAT Biosafety and Biosecurity Program – Established following the inadvertent anthrax release incident of 2015. Replaces the Biosurety Program and details how the Army will oversee, store, handle, and distribute Biological Select Agents and Toxins (BSAT).

The DoD wants to know that the biological contaminants (i.e. BSAT) are secure.

- DoD may employ their own scientists, biosafety regulators, risk assessment team, etc...
- Leverage expertise from CDC, FDA, NASA, USDA - Animal Plant Health Inspection Service (APHIS) for inspection.
 - Protocols (e.g. inactivation, sterilization, etc...)
 - Laboratories (DPG Staging areas, MSRF)

Federal agencies want to ensure that potential BSAT is secure and/or inactivated (sterilized). Sterilization standards and regulatory framework may be taken from medical device community.

Regulatory Framework for Serilants



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- Agencies responsible for sterilant oversight
 - EPA, FDA, and CDC
- Categorization based on associated risk of infection
 - **Critical** - Confer a high risk for infection if they are contaminated with any microorganism (surgical instruments, cardiac and urinary catheters).
 - **Semicritical** - Free from all microorganisms; small numbers of bacterial spores are permissible. Contact mucous membranes or nonintact skin (anesthesia equipment, some endoscopes).
 - **Noncritical** - Items are those that come in contact with intact skin but not mucous membranes (bedpans, blood pressure cuffs, crutches and computers).

EPA

- Regulates disinfectants used on environmental noncritical surfaces and gaseous sterilants
- Concludes the product can be used without causing “unreasonable adverse effects,”

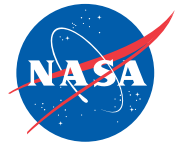
FDA

- Regulates liquid chemical sterilants used on critical and semicritical devices

CDC

- Inform the public current scientific evidence pertaining to these products (safety, efficacy, provide recommendations).

FDA Testing Guidelines (Established vs. Novel Methods) Medical Devices



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- A sterilization process should be verified before it is put into use in healthcare settings. *“Submission and Review of Sterility Information in Premarket Notification (510(k)) Submissions for Devices Labeled as Sterile Guidance for Industry and Food and Drug Administration Staff” – January 21, 2016*

Established - These are methods that have a long history of safe and effective use as demonstrated through multiple sources of information such as ample literature, clearances of 510(k)s or approvals of premarket approval (PMA) applications, and satisfactory QS inspections

- Dry Heat
- EtO
- Gamma
- Moist heat

Novel - A method that FDA has not reviewed and determined to be adequate to effectively sterilize the device for its intended use.

- Vaporized peracetic acid
- High intensity light or pulse light
- Microwave radiation
- Sound waves
- Ultraviolet light

Methodology Testing: Established vs. Novel (Where do we fit?)



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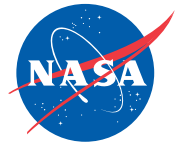
- **Established Testing**

- For the sterilization method, the sponsor should provide the following:
- Description of the sterilization method (data not needed at submission)
- Description of the sterilization chamber if not rigid, fixed
- Sterilization site
- In the case of radiation sterilization, the radiation dose
- For chemical sterilants (e.g., EO, H₂O₂), the maximum levels of sterilant residuals that remain on the device
- Description of the method used to validate the sterilization cycle
- State the sterility assurance level (SAL) of 10^{-3} – 10^{-6}
- Pyrogenicity testing (assess bacterial endotoxins)

- **Novel Testing**

- All of the above...
- Comprehensive description of the sterilization process;
- Method used to validate the sterilization cycle (e.g., the half-cycle method);
- Validation protocol
- Sterilization validation data (Include scientific literature).

How do we get there from here?



- Ensure our research and data meet minimum standards for acceptance for either Established or Novel techniques based on FDA guidances.
 - Proper positive and negative controls (where applicable). Test organisms.
 - Biological Indicators
 - Analogs
 - Microbe characterization
 - Testing methodologies should adhere to proven standards
 - Spore test; D-Values; fraction negative; Spearman-Kärber, etc...
 - V&V of Equipment (ISO standards)
 - Data storage and maintenance (e.g. industry standards?)
 - Electronic databases
 - Access
 - Peer-reviewed data (publications, conferences, etc...)
 - Transparency across all regulatory agencies/stakeholders (DoD, CDC, FDA, USDA, NASA). Proposed process is clear and rooted in good science.
 - Data should become a part of the Risk assessments